Are high-protein (>35%) hypocaloric diets safe and effective for long-term (>6 mo) weight loss and maintenance?

Conclusion

A moderate amount of evidence demonstrates that intake of dietary patterns with less than 45% calories from carbohydrate or more than 35% calories from protein are not more effective than other diets for weight loss or weight maintenance, are difficult to maintain over the long term, and may be less safe.

Grade: Moderate

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, click here.

Evidence Summary Overview

This conclusion is based on four articles published since 2004: three randomized controlled trials (RCTs) and one prospective cohort study (Benassi-Evans, 2009; Lim, 2009; Tay, 2008; Trichopoulou, 2007). Studies were conducted in the Australia, Greece, and Israel. Studies ranged in length from six months to 15 months. Studies also ranged in sample size from 33 to 22,944 subjects, and had drop-out rates from 0-34%. Diets tested ranged from 10-61% energy from fat, 17-50% energy from protein and 4-70% energy from carbohydrate (CHO). Three studies found no difference in long-term (more than six months) weight loss between high-protein (more than 35%) diets and diets differing in macronutrient proportion (Benassi-Evans, 2009; Lim, 2009; Tay, 2008).

Biomarkers improved in all macronutrient groups, including blood pressure (BP), fasting glucose, C-reactive protein (CRP) and triglycerides (TG). Biomarkers were associated with weight loss and did not vary by diet treatment. In addition, one study found that diets lower in CHO and higher in protein were associated with increased total and cardiovascular mortality (Trichopoulou, 2007).

Evidence Summary Paragraphs (4)

Randomized Controlled Trials (3)

Benassi-Evans et al, 2009 (positive quality) conducted a randomized clinical trial (RCT) in Australia to compare the effects of high-CHO, low-red-meat and high-protein, high-red-meat weight loss diets on genome stability in peripheral blood lymphocytes in overweight men. Subjects were assigned to one of two isocaloric, energy restricted diets: High CHO (17% protein, 58% CHO, 25% fat, N=17) or high protein, high red meat (35% protein, 40% CHO, 25% fat, N=16) diets for 12 weeks, followed by a 52-week weight maintenance period. Subjects met with the dietitian every two weeks for the first 12 weeks of the study, and then monthly until one year. Dietary intake for six days a month was assessed using checklists. The final sample included 33 men (mean age approximately 54 years; meanbody mass index (BMI) of 32kg/m^2), with 17 subjects in the high-CHO group and 16 subjects in the high-protein group. Both diets produced an average weight loss of 9.3±0.7kg after 12 weeks, with no further change after 52 weeks. There were also no significant (NS) differences between the diets with regards to any of the measures of genome stability and cell death in lymphocytes, including micronucleus frequency, nuclear buds, nucleoplasmic bridges, necrosis, apoptosis and nuclear division index.

Lim et al, 2009 (neutral quality) conducted an RCT in Australia to compare the changes in weight and other cardiovascular risk factors associated with three isocaloric energy-restricted diets to no-intervention control after one year. Subjects were randomly allocated to either very-low-CHO (VLC; 60% fat, 4% CHO, 36% protein; N=30), very-low-fat (VLF; 10% fat, 70% CHO, 20% protein; N=30), high-unsaturated fat (HUF; 30% fat, 20% protein, 50% CHO; N=30) with intensive support for three months followed by minimal support for 12 months, while the control group received no intervention. The final included 104 subjects (age 47±10 years; BMI of 32±6kg/m^2), with 30 subjects in the VLC group, 30 subjects in the VLF group, 30 subjects in the HUF group, and 23 subjects in the control group. Attrition rate at 15 months was 34%. Weight change at three months did not differ between diet groups, and was -8.0±2.8kg for VLC, -6.7±3.5kg for VLF, and -6.3±2.9kg for HUF. Weight change at 15 months did not differ between diet groups, and was -3.0±0.2kg for VLC, -2.0±0.1kg for VLF, and -3.7±0.1kg for HUF and was significantly different from controls (+0.8±5.0kg; $p<0.050$). When all groups were combined, weight loss at 15 months was significantly correlated to a higher protein intake (R=-0.38, P=0.0009), lower fat intake (R=0.31, P=0.037), and higher fiber intake (R=-0.30, P=0.038). There were no significant (NS) differences in weight change or cardiovascular risk factors between groups.

Tay et al, 2008 (positive quality) conducted an RCT in Australia to compare the effects on weight and cardiovascular disease (CVD) risk factors of moderate energy-restricted diets with different macronutrient composition. Subjects were randomly assigned to either a very-low-CHO, high-fat diet (VLCHF: 4% CHO, 35% protein, 61% fat) and a high-CHO, low-fat diet (HCLF: 46% CHO, 24% protein, 30% fat). Participants were provided with some food to enhance compliance with the dietary interventions, and three-day food records were kept every two weeks to assess dietary intake. After the first eight weeks, subjects assigned to the VLCHF diet were then given the option to increase CHO intake to less than 40g per day for the remaining 16 weeks, while subjects assigned to the HCLF diet were asked to restrict saturated fat intake to less than 10g per day for the study duration. The final sample included 88 subjects completed the trial (aged 18 to 65 years; mean BMI of 34kg/m^2), with 45 subjects in the VLCHF group and 43 in the HCLF group. Attrition rate was 19%. Weight loss was similar in both groups, as VLCHF subjects lost -11.9±6.3kg and HCLF subjects lost -10.1±5.7kg. Also, blood pressure, CRP, fasting glucose and insulin decreased similarly in both diet groups. However, the VLCHF diet produced greater decreases in triacylglycerols (P=0.01) and increases in HDL-C (P=0.002), while the HCLF diet produced a greater decrease in LDL-C ($P<0.001$).

Prospective Cohort Study (1)

Trichopoulou et al, 2007 (positive quality) analyzed data from Greek participants (N=22,944) in a prospective cohort study [European Prospective Investigation in Cancer and Nutrition (EPIC)] to examine the mortality of individuals according to their CHO and protein intake. Dietary data was collected using a validated, interviewer-administered, 150-item food-frequency questionnaire (FFQ) focused on the year prior to enrollment. Mortality was determined using date and cause of death from death certificates and other official sources. A LC/HP (low- CHO, high-protein) score was calculated for each subject, with a higher score implying higher protein and lower CHO intake. Results showed that an increasing LC/HP score was significantly associated with mortality [1.08 (1.03, 1.13); P=0.001] (adjusted for sex, age, years of schooling, smoking, BMI, physical activity, ethanol intake and total energy intake). Individuals with habitual diets low in CHO and high in protein tend to have higher overall mortality, compared to individuals with habitual diets high in CHO and low in protein. This increase in mortality was not concentrated to particular causes, but was significant only with respect to cardiovascular deaths.

View table in new window

Author, Year, Study Design, Class, Rating	Population	Intervention (Initial / Intense Phase)	Intervention (Follow-Up / Maintenance Phase)	Macronutrient Composition of Diet	Weight Outcomes (End of Initial / Intense Phase)	Weight Outcomes (End of F/U / Maintenance Phase)	Safety Outcomes
Benassi-Evans et al 2009 Study Design: Randomized Clinical Trial Class: A Rating:	N=33 men. • N=17 high-CHO group • N=16 high-protein group. Age: 54 years. BMI: 32kg/m^2.	Subjects were assigned to one of two isocaloric, energy-restricted diets: High CHO, low red meat or high protein, high red meat diets for 12 weeks. Subjects met with the dietitian every two weeks for the first 12 weeks of the study. Dietary intake for six days a month was assessed using checklists.	The initial 12-week intervention was followed by a 52-week weight maintenance period, during which time subjects met with the dietitian monthly.	High-CHO diet: 58% CHO, 25% protein, 17% fat. High-protein diet: 40% CHO, 25% protein, 35% fat.	Both diets produced an average weight loss of 9.3±0.7kg after 12 weeks.	No further weight Δ occurred in the 52-week weight maintenance period.	There were NS differences between the diets with regards to any of the measures of genome stability and cell death in lymphocytes, including micronucleus frequency, nuclear buds, nucleoplasmic bridges, necrosis, apoptosis and nuclear division index.
Lim et al 2009 Study Design: Randomized Controlled Trial Class: A Rating:	N=104 subjects. • N=30 VLC group • N=30 VLF group • N=30 HUF group • N=23 control group. Age: 47 years. BMI: 32kg/m^2. Attrition rate at 15 months: 34%.	Subjects were randomly allocated to either very-low-CHO (VLC), very-low-fat (VLF), high-unsaturated fat (HUF) with intensive support for three months, while the control group received no intervention.	The intensive three-month initial phase was followed by minimal support for 12 months.	VLC: 4% CHO, 60% protein, 35% fat. VLF: 70% CHO, 10% protein, 20% fat. HUF: 50% CHO, 30% protein, 20% fat.	Weight Δ at three months did not differ between diet groups and was -8.0±2.8kg for VLC, -6.7±3.5kg for VLF and -6.3±2.9kg for HUF.	Weight change at 15 months did not differ between diet groups, and was -3.0±0.2kg for VLC, -2.0±0.1kg for VLF and -3.7±0.1kg for HUF, and was significantly different from controls (+0.8±5.0kg; P<0.050). For all groups combined, weight loss at 15 months was significantly correlated to a higher protein intake (R=-0.38, P=0.0009), lower fat intake (R=0.31, P=0.037) and higher fiber intake (R=-0.30, P=0.038).	At 15 months, there were no significant differences in weight change or cardiovascular risk factors between groups.

Tay et al 2008 Study Design: Randomized Clinical Trial Class: A Rating:	N=88 subjects. • N=45 VLCHF group • N=43 HCLF group. Age: 18 to 65 years. BMI: 34kg/m2. Attrition rate: 19%.	Subjects were randomly assigned to either a very-low-CHO, high-fat diet (VLCHF) and a high-CHO, low-fat diet (HCLF). Participants were provided with some food to enhance compliance with the dietary interventions, and three-day food records were kept every two weeks to assess dietary intake.	Not applicable.	VLCHF: 4% CHO, 61% protein, 35% fat. HCLF: 46% CHO, 30% protein, 24% fat.	Weight loss was similar in both groups, as VLCHF subjects lost -11.9±6.3kg and HCLF subjects lost -10.1±5.7kg.	Not applicable.	Blood pressure, CRP, fasting glucose and insulin ↓ similarly in both diet groups. The VLCHF diet produced greater ↓ in triacylglycerols (P=0.01) and ↑ in HDL-C (P=0.002), while the HCLF diet produced a greater ↓ in LDL-C (P<0.001).
Trichopoulou A, Psaltopoulou T et al, 2007 Study Design: Prospective Cohort Study Class: B Rating:	N=22,944. Women and men aged 20 to 86 years at the time of enrollment between 1993 and 1999.	Prospective cohort study in which follow-up was performed from 1993 to 2003 to evaluate the effects of diet on mortality. Participants were distributed by increasing deciles according to protein intake or CHO intake, as well as by an additive score (LC/HP score) generated by increasing decile intake of protein and decreasing decile intake of CHO.	Not applicable.	A LC/HP (low CHO, high protein) score was calculated for each subject based on CHO and protein intake estimated using a 150-item FFQ. A high score implies higher-protein, lower-CHO intake.	Not applicable.	Not applicable.	An increasing LC/HP score was significantly associated with mortality [1.08 (1.03, 1.13); P=0.001] (adjusted for sex, age, years of schooling, smoking, BMI, physical activity, ethanol intake and total energy intake). This ↑ in mortality was not concentrated to particular causes, but was significant only with respect to cardiovascular deaths.

Research Design and Implementation Rating Summary
For a summary of the Research Design and Implementation Rating results, click here.

Worksheets

Benassi-Evans B, Clifton PM, Noakes M, Keogh JB, Fenech M. High protein-high red meat versus high carbohydrate weight loss diets do not differ in effect on genome stability and cell death in lymphocytes of overweight men. *Mutagenesis.* 2009;24(3):271-277.

Lim SS, Noakes M, Keogh JB, Clifton PM. Long-term effects of a low carbohydrate, low fat or high unsaturated fat diet compared to a no-intervention control. *Nutr Metab Cardiovasc Dis.* 2009 Aug 17.

Tay J, Brinkworth GD, Noakes M, Keogh J, Clifton PM. Metabolic effects of weight loss on a very-low-carbohydrate diet compared with an isocaloric high-carbohydrate diet in abdominally obese subjects. *J Am Coll Cardiol.* 2008;51(1):59-67.

Trichopoulou A, Psaltopoulou T, Orfanos P, Hsieh CC, Trichopoulos D. Low-carbohydrate-high-protein diet and long-term survival in a general population cohort. *Eur J Clin Nutr.* 2007 May; 61(5): 575-581.